L3 ANSWER 3 OF 21 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001683638 MEDLINE
DOCUMENT NUMBER: 21548044 PubMed ID: 11689490
TITLE: CAG repeat instability at **SCA2** locus: anchoring CAA interruptions and linked single nucleotide **polymorphisms**.
AUTHOR: Choudhry S; Mukerji M; Srivastava A K; Jain S; Brahmachari S K
CORPORATE SOURCE: Functional Genomics Unit, Centre for Biochemical Technology
(CSIR), Mall Road, Delhi, India.
SOURCE: HUMAN MOLECULAR GENETICS, (2001 Oct 1) 10 (21) 2437-46.
Journal code: 9208958. ISSN: 0964-6906.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF330028; GENBANK-AF330029; GENBANK-AF330030; GENBANK-AF330031; GENBANK-AF330032; GENBANK-AF330033
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011204
Last Updated on STN: 20020125
Entered Medline: 20020117

AB Spinocerebellar ataxia 2 (**SCA2**) is an autosomal dominant neurodegenerative disorder that results from the expansion of a cryptic CAG repeat within the exon 1 of the **SCA2** gene. The CAG repeat in normal individuals varies in length from 14 to 31 repeats and is frequently interrupted by one or more CAA triplets, whereas the expanded alleles contain a pure uninterrupted stretch of 34 to 59 CAG repeats. We have previously reported the presence of a limited pool of 'ancestral' or 'at risk' haplotypes for the expanded **SCA2** alleles in the Indian population. We now report the identification of two novel single nucleotide **polymorphisms** (**SNPs**) in exon 1 of the **SCA2** gene and their characterization in 215 normal and 64 expanded chromosomes. The two biallelic **SNPs** distinguished two haplotypes, GT and CC, each of which formed a predominant haplotype associated with normal and expanded **SCA2** alleles. All the expanded alleles segregated with CC haplotype, which otherwise was associated with only 29.3% of the normal chromosomes. CAA interspersion analysis revealed that majority of the normal alleles with CC haplotype were either pure or lacked the most proximal 5' CAA interruption. The repeat length variation at **SCA2** locus also appeared to be polar with changes occurring mostly at the 5' end of the repeat. Our results demonstrate that CAA interruptions play an important role in conferring stability to **SCA2** repeat and their absence predisposes alleles towards instability and pathological expansion. Our study also provides new haplotypes associated with **SCA2** that should prove useful in further understanding the mutational history and mechanism of repeat instability at the **SCA2** locus.

L3 ANSWER 11 OF 21 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999158295 MEDLINE
DOCUMENT NUMBER: 99158295 PubMed ID: 10051008
TITLE: Analysis of spinocerebellar ataxia type 2 gene and haplotype analysis: (CCG)1-2 **polymorphism** and contribution to founder effect.
AUTHOR: Mizushima K; Watanabe M; Kondo I; Okamoto K; Shizuka M; Abe

K; Aoki M; Shoji M
CORPORATE SOURCE: Department of Neurology, Gunma University School of Medicine, Maebashi, Japan.
SOURCE: JOURNAL OF MEDICAL GENETICS, (1999 Feb) 36 (2) 112-4.
Journal code: 2985087R. ISSN: 0022-2593.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 20000303
Entered Medline: 19990512

AB Spinocerebellar ataxia type 2 is a familial spinocerebellar ataxia with autosomal dominant inheritance. The gene responsible was recently cloned and this disorder was found to be the result of a CAG expansion in its open reading frame. We analysed 13 **SCA2** patients in seven unrelated families in Gunma Prefecture, Japan. In four of the seven families, we detected CCG or CCGCCG interruptions in only the expanded alleles. Cosegregation of these **polymorphisms** with **SCA2** patients was established within each family. Together with the results of haplotype analyses, we considered that at least two founders were present in our area and that these (CCG)1-2 **polymorphisms** may make analysis of founder effects easier. By sequencing analysis we found that although the number of the long CAG repeat varied in each subclone of expanded alleles, these **polymorphisms** did not change their configuration. This finding suggests that CCG or CCGCCG sequences are stable when surrounded by the long CAG repeat and a single CAG. Moreover, the presence of these **polymorphisms** may lead to miscounting the repeat size by conventional estimation using a size marker such as an M13 sequencing ladder. Therefore we should consider these **polymorphisms** and accurately determine the repeat size by sequencing.

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